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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/904,710	07/12/2001	Narasimhaswamy Manjunath	GFN- 5339DV	4467

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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 04/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/904,710	MANJUNATH ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,26-32 and 34* is/are pending in the application.

4a) Of the above claim(s) *30 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,26-29,32 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☒ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission, filed on 3/25/05, has been entered.

Applicant's amendment, filed 3/25/05, has been entered.
Claims 1 and 28 have been amended.
Claim 35 has been canceled. Claims 2-25 and 33 have been canceled previously.

Claims 1, 26-32 and 34 are pending.

Claims 30-31 have been withdrawn from consideration as they read on the non-elected inventions and species.

Applicant's election with traverse of Group II (claims 1, 2, 4 and 26-34), drawn to methods of inhibiting T cell cytotoxicity with PSGL-specific antibodies and the species autoimmune diseases in the Election filed 3/1/04 has been acknowledged.

Claims 1, 26-29, 32 and 34 are under consideration as they read on the elected invention.

2. Applicant is reminded of the proper Content of the Specification

Content of Specification

(a) Title of the Invention: See 37 CFR 1.72(a) and MPEP § 606. The title of the invention should be placed at the top of the first page of the specification unless the title is provided in an application data sheet. The title of the invention should be brief but technically accurate and descriptive, preferably from two to seven words may not contain more than 500 characters.

(b) Cross-References to Related Applications: See 37 CFR 1.78 and MPEP § 201.11.

(c) Statement Regarding Federally Sponsored Research and Development: See MPEP § 310.

(d) The Names Of The Parties To A Joint Research Agreement: See 37 CFR 1.71(g).

(e) Incorporation-By-Reference Of Material Submitted On a Compact Disc: The specification is required to include an incorporation-by-reference of electronic documents that are to become part of the permanent United States Patent and Trademark Office records in the file of a patent application. See 37 CFR 1.52(e) and MPEP § 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more

than 50 pages of text were permitted as electronic documents on compact discs beginning on September 8, 2000.

Or alternatively, Reference to a "Microfiche Appendix": See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.

(f) Background of the Invention: See MPEP § 608.01(c). The specification should set forth the Background of the Invention in two parts:

(1) Field of the Invention: A statement of the field of art to which the invention pertains. This statement may include a paraphrasing of the applicable U.S. patent classification definitions of the subject matter of the claimed invention. This item may also be titled "Technical Field."

(2) Description of the Related Art including information disclosed under 37 CFR 1.97 and 37 CFR 1.98: A description of the related art known to the applicant and including, if applicable, references to specific related art and problems involved in the prior art which are solved by the applicant's invention. This item may also be titled "Background Art."

(g) Brief Summary of the Invention: See MPEP § 608.01(d). A brief summary or general statement of the invention as set forth in 37 CFR 1.73. The summary is separate and distinct from the abstract and is directed toward the invention rather than the disclosure as a whole. The summary may point out the advantages of the invention or how it solves problems previously existent in the prior art (and preferably indicated in the Background of the Invention). In chemical cases it should point out in general terms the utility of the invention. If possible, the nature and gist of the invention or the inventive concept should be set forth. Objects of the invention should be treated briefly and only to the extent that they contribute to an understanding of the invention.

(h) Brief Description of the Several Views of the Drawing(s): See MPEP § 608.01(f). A reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74.

(i) Detailed Description of the Invention: See MPEP § 608.01(g). A description of the preferred embodiment(s) of the invention as required in 37 CFR 1.71. The description should be as short and specific as is necessary to describe the invention adequately and accurately. Where elements or groups of elements, compounds, and processes, which are conventional and generally widely known in the field of the invention described and their exact nature or type is not necessary for an understanding and use of the invention by a person skilled in the art, they should not be described in detail. However, where particularly complicated subject matter is involved or where the elements, compounds, or processes may not be commonly or widely known in the field, the specification should refer to another patent or readily available publication which adequately describes the subject matter.

(j) Claim or Claims: See 37 CFR 1.75 and MPEP § 608.01(m). The claim or claims must commence on separate sheet or electronic page (37 CFR 1.52(b)(3)). Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation. There may be plural indentations to further segregate subcombinations or related steps. See 37 CFR 1.75 and MPEP § 608.01(i)-(p).

(k) Abstract of the Disclosure: See MPEP § 608.01(f). A brief narrative of the disclosure as a whole in a single paragraph of 150 words or less commencing on a separate sheet following the claims. In an international application which has entered the national stage (37 CFR 1.491(b)), the applicant need not submit an abstract commencing on a separate sheet if an abstract was published with the international application under PCT Article 21. The abstract that appears on the cover page of the pamphlet published by the International Bureau (IB) of the World Intellectual Property Organization (WIPO) is the abstract that will be used by the USPTO. See MPEP § 1893.03(e).

(l) Sequence Listing. See 37 CFR 1.821-1.825 and MPEP §§ 2421-2431. The requirement for a sequence listing applies to all sequences disclosed in a given application, whether the sequences are claimed or not. See MPEP § 2421.02.

The Brief Description of the Drawings is not arranged properly in the instant application.

Applicant is required to comply with the proper arrangement of the Specification.

3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Appliicant's amended claims, filed 3/25/05, have obviated the previous rejection under 35 U.S.C. § 112, first paragraph, written description / new matter with respect to the recitation of "determining said mammalian subject would benefit from inhibition of a cytotoxic T cell response" and "determining the dose or dose range of an antibody directed to PSGL".

5. Claims 1, 26-29, 32 and 34 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

The specification as originally filed does not provide support for the invention as now claimed: "determining said mammalian subject has a condition associated with abnormal generation or function of cytotoxic T lymphocytes" (see claims 1 and 28).

Applicant's amendment, filed 3/25/05, directs support to page 34, lines 5-10 of the instant specification for the newly added "limitation".

However, the listing of References on page 34 of the instant specification as filed does not provide a sufficient written description nor set forth the metes and bounds of the claimed "limitations.

The specification does not provide sufficient blazemarks nor direction for the instant methods encompassing the above-mentioned "limitation", as currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action.

Alternatively, applicant is invited to provide sufficient written support for the Alimitations≅ indicated above. See MPEP 714.02 and 2163.06

6. Applicant's amended claims, filed 3/25/05, have obviated the previous rejection under 35 U.S.C. § 112, second paragraph, indefiniteness with respect to the recitation of "determining said mammalian subject would benefit from inhibition of a cytotoxic T cell response".

7. Claims 1, 26-29, 32 and 34 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 26-29, 32 and 34 are indefinite in the recitation of "determining said mammalian subject has a condition associated with abnormal generation or function of cytotoxic T lymphocytes" (see claims 1 and 28) because the determination is not defined by the claims; the specification does not provide a standard for ascertaining the requisite degree.

For example, what defines "abnormal generation or function of cytotoxic T lymphocytes", what defines "associated" and, of course, what are assays or endpoints being determined by the claimed method step is ambiguous and ill-defined. One of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless --

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

10. Claims 1, 26-29 and 32-34 are rejected under 35 U.S.C.§ 102(e) as being anticipated by Cummings et al. (U.S. Patent No. 6,667,036 B2) (see entire document) and in further evidence that rheumatoid arthritis was known to be a condition associated with abnormal generation or function of cytotoxic T lymphocytes by Brenner et al. (U.S. Patent No. 5,747,036).

Applicant's arguments filed 3/25/05 have been fully considered but are not found convincing.

Applicant asserts that the instant invention is based, at least in part, on the realization that anti-PSGL-1 antibodies inhibit differentiation of activated proliferating T cells into CTLs and asserts that Cummings fails to teach or suggest determining that a mammalian subject has a condition associated with abnormal generation or function of CTLs, as recited in the instant claims.

Even though applicant has amended the claims to recite "determining said mammalian subject has a condition associated with abnormal generation or function of cytotoxic T lymphocytes" in step (a) of claims 1 and 28,

the broadest reasonable interpretation of this step is simply determining that the mammalian subject has a condition such as rheumatoid arthritis and knowing that such a condition such as rheumatoid arthritis has been associated with abnormal generation or function of CTLs.

The claims do not require an actual determination of CTL function per se.

Further, as pointed out above, the recitation of step (a) in claims 1 and 28 are subject to a rejection under 35 USC 112, second paragraph, indefiniteness as well.

Brenner et al. has been provided as an evidentiary reference to support that the ordinary artisan recognized that rheumatoid arthritis was known to be associated with the generation and function of cytotoxic T lymphocytes at the time the invention was made.

For example, Brenner et al. teaches the presence and role of activated $CD8^+$ cytotoxic T lymphocytes in rheumatoid arthritis (e.g. see entire document, including Background of the Invention, Summary of the Invention and Detailed Description, including Treatment of Rheumatoid Arthritis with Anti-Vα12.1-Antibodies on columns 15-17).

Therefore, applicant's arguments and the examiner's rebuttal are essentially the same of record, as applicant relies upon limitations not necessarily claimed (e.g. no actual method steps as well as indefiniteness) and the examiner relies upon broadest reasonable interpretation of the claims and inherency of treating the same patients with the same active ingredients in the same or nearly the same therapeutic regimens to treat rheumatoid arthritis patients with anti-PSGL-1 antibodies.

Applicant has acknowledged that Cummings discusses administration of an anti-PSGL antibody includes an assessment of a clinical response. However, applicant asserts that Cummings provides no teaching or suggestion of determining a mammalian subject would benefit from inhibition of cytotoxic T cell response.

The following of record is reiterated for applicant's convenience.

Cummings et al. teach methods of inhibiting various inflammatory conditions including rheumatoid arthritis (e.g. see column 18, paragraph 6 and column 20, paragraph 1) with antibodies that bind PSGL (see Clinical Applications on columns 18-21 and Claims, particularly Claim 1). Given that rheumatoid arthritis is an autoimmune disease, the prior art teaching of a species reads on the claimed genus. Monoclonal antibodies and fragments thereof and pharmaceutical compositions are taught as well (e.g. see column 5, paragraph 1 and columns 30-31).

Although the reference is silent about recite "determining said mammalian subject has a condition associated with abnormal generation or function of cytotoxic T lymphocytes", it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). "{i}t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable." In re Woodruff, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See MPEP 2145.

As pointed out herein, the claims are read broadly on treating a patient with rheumatoid arthritis and recognizing that rheumatoid arthritis was "a condition associated with abnormal generation or function of cytotoxic T lymphocytes" and not on an explicit method step of detecting or assaying CTL function per se.

Applicant's arguments are not found persuasive.

11. Claims 1, 26-29, 32 and 34 are rejected under 35 U.S.C. § 102(e) as being anticipated by Larsen et al. (U.S. Patent No. 6,277,975) (see entire document) and in further evidence that rheumatoid arthritis was known to be a condition associated with abnormal generation or function of cytotoxic T lymphocytes by Brenner et al. (U.S. Patent No. 5,747,036).

Applicant's arguments filed 3/25/05 have been fully considered but are not found convincing.

Applicant asserts that the instant invention is based, at least in part, on the realization that anti-PSGL-1 antibodies inhibit differentiation of activated proliferating T cells into CTLs and asserts that Cummings fail to teach or suggest determining that a mammalian subject has a condition associated with abnormal generation or function of CTLs, as recited in the instant claims.

Even though applicant has amended the claims to recite "determining said mammalian subject has a condition associated with abnormal generation or function of cytotoxic T lymphocytes" in step (a) of claims 1 and 28,

the broadest reasonable interpretation of this step is simply determining that the mammalian subject has a condition such as rheumatoid arthritis and knowing that such a condition such as rheumatoid arthritis has been associated with abnormal generation or function of CTLs.

The claims do not require an actual determination of CTL function per se.

Further, as pointed out above, the recitation of step (a) in claims 1 and 28 are subject to a rejection under 35 USC 112, second paragraph, indefiniteness as well.

Brenner et al. has been provided as an evidentiary reference to support that the ordinary artisan recognized that rheumatoid arthritis was known to be associated with the generation and function of cytotoxic T lymphocytes at the time the invention was made.

For example, Brenner et al. teaches the presence and role of activated $CD8^+$ cytotoxic T lymphocytes in rheumatoid arthritis (e.g. see entire document, including Background of the Invention, Summary of the Invention and Detailed Description, including Treatment of Rheumatoid Arthritis with Anti-Vα12.1-Antibodies on columns 15-17).

Therefore, applicant's arguments and the examiner's rebuttal are essentially the same of record, as applicant relies upon limitations not necessarily claimed (e.g. no actual method steps as well as indefiniteness) and the examiner relies upon broadest reasonable interpretation of the claims and inherency of treating the same patients with the same active ingredients in the same or nearly the same therapeutic regimens to treat rheumatoid arthritis patients with anti-PSGL-1 antibodies.

The following of record is reiterated for applicant's convenience.

Larsen et al. teach methods of treating a variety of conditions, including inflammatory disorders and autoimmune diseases (see column 17, paragraph 1) with antibodies that neutralize PSGL, including monoclonal antibodies and antibody fragments (e.g, see column 3-4 of the Summary of the Invention and columns 9 and 19 –20 of the Detailed Description) in therapeutically effective amounts and pharmaceutical compositions (e.g. see columns 17-19).

Further, it is noted that column 18, paragraph 2, appears to be the same or nearly the same disclosure of "effective amounts" as disclosed on page 4 of the instant specification.

"As used herein, the term "therapeutically effective amount" means the total amount of each active component of the pharmaceutical composition or method that is sufficient to show a meaningful patient benefit, i.e. healing of chronic conditions characterized by P-selectin or E-selectin-mediated cellular adhesion or increase in rate of healing of such conditions. When applied to an individual active ingredient, administered alone, the term refers to that ingredient alone. When applied to a combination, the term refers to combined amounts of the active ingredients that result in the therapeutic effect whether administered in combination serially or simultaneously."

In addition, Larsen et al. teach dosage amounts (e.g. about 0.1 µg to about 100 mg per kg body weight) as well as dosages determined by the attending physician for the individual patient (e.g. see column 19, paragraph 2) as well as the properties of neutralizing antibodies (e.g. see column 20, paragraph 2)

Although the reference is silent about the inhibition of a cytotoxic T lymphocyte response, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). "{i}t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable." In re Woodruff, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

As pointed out herein, the claims are read broadly on treating a patient with rheumatoid arthritis and recognizing that rheumatoid arthritis was "a condition associated with abnormal generation or function of cytotoxic T lymphocytes" and not on an explicit method step of detecting or assaying CTL function per se.

Applicant's arguments are not found persuasive

12. Claims 1, 26-29, 32 and 34 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Cummings et al. (U.S. Patent No. 6,667,036 B2) AND/OR Larsen et al. (U.S. Patent No. 6,277,975) in view of Snapp et al. (Blood 91 : 154-164 (1998), Diacovo et al. (J. Exp. Med. 183: 1193- 1203 (1996), Raychaudhuri et al. (U.S. Patent No. 6,270,769 B1) and Rooney et al. (U.S. Patent No. 56,962,318) essentially for the reasons of record and further in view of newly added Brenner et al. (U.S. Patent No. 5,747,036).

Applicant's arguments, filed 3/25/05, have been fully considered but are not found convincing essentially for the reasons of record.

Applicant asserts that there was no motivation to use Snapp and Diacovo in the same rejection and asserts that one skilled in the art would not expect that a PSGL antibody would necessarily inhibit binding of $CD8^+$ α/β T cells to P selectin where it is the $CD8^-$ γ/δ T cells which do not necessarily express PSGL that show enhance P selectin binding.

In addition to applicant's mischaracterization of the referenced teaching, Snapp et al. concludes that: "In summary, using a novel MoAb directed against the functionally essential tyrosine sulfation motif of human PSGL-1, we show that PSGL-1 is expressed on all circulating leukocytes, including neutrophils, monocytes, all subsets of T cells, NK cells, and B cells and is the principal or sole ligand for P-selectin on at least T cells and neutrophils." See page 163, column 1, paragraph 1).

In contrast to applicant's assertions of a lack of motivation, Snapp et al. teach that all T cells, including $CD8^+$ T cells express high levels of PSGL-1 (see entire document, including Abstract; page 155, column 1, lines 1-3) and that PSGL-1 is the principal or sole ligand for P-selectin on T cells (e.g. see page 162, column 1, paragraph 3).

Diacovo et al. teach PSGL mediates P-selectin-dependent adhesion of myeloid cells, is also present on α/β T cells and may serve a similar function (see entire document, including page 1194, column 1, paragraph 1). Also, anti-PSGL-1 antibodies have been shown to completely inhibit binding of purified P-selectin to neutrophils as well as to peripheral blood T lymphocytes (page 1200, column 2, lines 2-5). IT appears that functional PSGL-1 may be induced during antigen-mediated naïve virgin-to-memory T cell conversion in secondary lymphoid tissue (see page 1200, column 2, lines14-17).

In addition, in contrast to applicant's comments concerning the secondary references of Snapp et al., Diacovo et al., Rooney et al. and Raychaudhuri et al.; once a prima facie case of obviousness has been made the burden of going further is shifted to applicant. In re Keller, 642 F.2d 4B, 208 USPQ 871, 882 (CCPA 1981). This applicant has not done, but rather argues the references individually and not their combination. One cannot show non-obviousness by attacking references individually where the rejections are based on a combination of references. In re Young 403 F.2d 759, 150 USPQ 725 (CCPA 1968). See MPEP 2145.

Brenner et al. has been provided to add further support that the ordinary artisan recognized that rheumatoid arthritis was known to be associated with the generation and function of cytotoxic T lymphocytes at the time the invention was made.

For example, Brenner et al. teaches the presence and role of activated $CD8^+$ cytotoxic T lymphocytes in rheumatoid arthritis (e.g. see entire document, including Background of the Invention, Summary of the Invention and Detailed Description, including Treatment of Rheumatoid Arthritis with Anti-Vα12.1-Antibodies on columns 15-17). Here, Brenner et al. also teach diagnosing patients with autoimmune diseases such as rheumatoid arthritis to determine the presence and function of CTLs (e.g., see Diagnosing Rheumatoid Arthritis with Arthritis with Anti-Vα12.1-Antibodies on columns 11-15).

The following of record is reiterated for applicant's convenience.

Cummings et al. teach methods of inhibiting various inflammatory conditions including rheumatoid arthritis (e.g. see column 18, paragraph 6 and column 20, paragraph 1) with antibodies that bind PSGL (see Clinical Applications on columns 18-21 and Claims, particularly Claim 1). Given that rheumatoid arthritis is an autoimmune disease, the prior art teaching of a species reads on the claimed genus. Monoclonal antibodies and fragments thereof and pharmaceutical compositions are taught as well (e.g. see column 5, paragraph 1 and columns 30-31).

Larsen et al. teach methods of treating a variety of conditions, including inflammatory disorders and autoimmune diseases (see column 17, paragraph 1) with antibodies that neutralize PSGL, including monoclonal antibodies and antibody fragments (e.g., see column 3-4 of the Summary of the Invention and columns 9 and 19 –20 of the Detailed Description) in therapeutically effective amounts and pharmaceutical compositions (e.g. see columns 17-19).

Cummings et al. and Larsen et al. differ from the claimed methods by not disclosing "determining said mammalian subject would benefit from inhibition of a cytotoxic T cell response" as a separate step.

Snapp et al. teach that all T cells, including $CD8^+$ T cells express high levels of PSGL-1 (see entire document, including Abstract; page 155, column 1, lines 1-3) and that PSGL-1 is the principal or sole ligand for P-selectin on T cells (e.g. see page 162, column 1, paragraph 3).

Diacovo et al. teach PSGL mediates P-selectin-dependent adhesion of myeloid cells, is also present on α/β T cells and may serve a similar function (see entire document, including page 1194, column 1, paragraph 1). Also, anti-PSGL-1 antibodies have been shown to completely inhibit binding of purified P-selectin to neutrophils as well as to peripheral blood T lymphocytes (page 1200, column 2, lines 2-5). IT appears that functional PSGL-1 may be induced during antigen-mediated naïve virgin-to-memory T cell conversion in secondary lymphoid tissue (see page 1200, column 2, lines14-17).

Therefore, Snapp et al. and Diacovo et al. teach that $CD8^+$ T cells, wherein the hallmark of said $CD8^+$ T cells is their ability as cytotoxic T lymphocytes (CTL) to kill other cells. Activated cytotoxic T lymphocytes are derived from inactive CTL precursors. CTLs are important in immunological responses, including responses to tumors and graft rejection.

Therefore, it would have obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of Snapp et al. and Diacovo et al. to those of Cummings et al. AND/OR Larsen et al. to determine the ability of anti-PSGL-1 antibodies to modulate or inhibit the functions, including CTL functions of said $CD8^+$ T cells. Given the number and types of diseases and conditions targeted by Cummings et al. and Larsen et al., one of ordinary skill in the art would have been motivated to monitor the ability of anti-PSGL-1 antibodies to inhibit various immune responses, including the immune responses of cells expressing PSGL-1, including $CD8^+$ T cells.

Raychaudhuri et al. teach the known methods of determining CTL function (see entire document).

Rooney et al. similarly teach methods of monitoring CTL function (see entire document), including testing blocking antibodies (e.g. see column 32, paragraph 1).

Therefore, both Raychaudhuri et al. and Rooney et al. provide the known methods of testing CTL responses, including in response to immunosuppressive antibodies.

The teachings of newly added Brenner et al. are set forth above and provide further motivation and expectation of success that in treating rheumatoid arthritis, the ordinary artisan recognized the role of T cells, including CTLS, and that is was well within the purview of the ordinary artisan to detect or diagnose the presence and function of CTLs in patients with rheumatoid arthritis and to treat rheumatoid arthritis with an effort to inhibit CTL function is said patients at the time the invention was made.

Given the teachings of the combination of references that anti-PSGL-1 inhibit a variety of immune responses and was useful in treating a number of diseases and conditions and the ability of said anti-PSGL-1 antibodies that inhibit a number of interactions and functions of targeted cells, a person of ordinary kill in the art would have been motivated to monitor the effects of anti-PSGL-1 antibodies on the targeted cells, including the $CD8^+$ T cells, in order to determine the effects of such anti-PSGL-1 treatment at the time the invention was made.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary

Applicant's arguments have not been found persuasive.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

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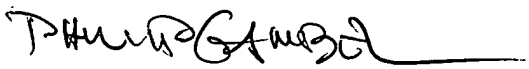

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